Research Article

# Sex dimorphism in the distribution of adipose tissue and its influence on proinflammatory adipokines and cardiometabolic profiles in motor complete spinal cord injury

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**Objective:** We aimed to examine the influence of sex on the distribution of adipose tissue, as well as proinflammatory adipokine and cardiometabolic profiles, in chronic motor complete spinal cord injury (SCI).
**Design:** Cross-sectional and correlational study.
**Setting:** Academic rehabilitation hospital.
**Participants:** Forty-seven individuals with chronic motor complete SCI classified according to sex (males: age 44.0 ± 10.9 y, body mass index (BMI) 27.2 ± 5.8, level of injury (LOI) C4 - L1; females: 42.0 ± 13.5 y, BMI 27.8 ± 6.6, LOI C4 - T11).
**Intervention:** Not applicable.
**Outcome Measures:** Visceral (VAT), subcutaneous (SAT), and total trunk (TTAT) adipose tissue volumes were assessed utilizing magnetic resonance imaging and a VAT:SAT ratio was calculated. Proinflammatory adipokines (tumor neurosis factor-α, interleukin-6, plasminogen activator inhibitor-1, thrombin-activatable fibrinolysis inhibitor, and high sensitivity c-reactive protein) and cardiovascular, carbohydrate, and lipid profiles were evaluated according to standard techniques.
**Results:** VAT and VAT:SAT ratio were significantly greater in male participates with SCI ($P \leq 0.002$), while SAT volume was significantly greater in female participants with SCI ($P = 0.001$). No difference was noted in TTAT between groups ($P = 0.341$). Male participants with SCI demonstrated lower high-density lipoprotein-cholesterol (HDLC) profiles and an elevated total cholesterol to HDLC ratio ($P \leq 0.003$) compared with females. No other significant differences were found between groups concerning cardiometabolic profiles or proinflammatory adipokines; however, males exhibited poorer profiles overall. Proinflammatory adipokines significantly correlated with adipose tissue depots by sex ($P < 0.05$).
**Conclusion:** The results show that sex influences the distribution of adipose tissue, and may influence proinflammatory and cardiometabolic profiles following SCI. The findings of this study highlight the need for further research with dietary modification and exercise to decrease health risks.

**Keywords:** Spinal cord injury, Obesity, Adipose tissue, sex, Proinflammatory adipokines

## Introduction

As a consequence of neurological dysfunction, alterations in body composition place individuals with a spinal cord injury (SCI) at almost two times greater risk than the able-bodied (AB) population for cardiovascular disease and type two diabetes mellitus.[1,2] This is believed to be driven, in part, by a higher rate of obesity that exceeds

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66% in the SCI population, as well as metabolic dysfunction that follows the injury.[2] Obesity results from an imbalance of energy intake and expenditure and is characterized by the accumulation of adipose tissue in both visceral and subcutaneous depots. The distribution of adipose tissue has been shown to be a stronger predictor of health risk compared to overall, whole-body excessive adiposity.[2] Literature has described proportional increases in visceral adipose tissue (VAT) and cardiometabolic dysfunction, while subcutaneous adipose tissue (SAT) is associated with reduced cardiometabolic complications and is thought to be protective against adverse health risks.[3,4]

The differences in the distribution of adipose tissue and cardiometabolic health and their role in morbidity have been strongly linked to sex.[3,5] Differences in VAT and SAT are still emerging, but are largely thought to relate to sex-specific traits such as levels of estrogen and testosterone.[3] These characteristics of adipose tissue have been investigated in the AB population, but due to the unique pathophysiology of SCI, these characteristics of adipose tissue remain poorly understood.[2,6] Much of the literature examining body composition and metabolism following SCI has disproportionally focused on evaluating men with SCI, despite the increasing number of women with SCI in recent years.[7,8] In fact, the majority of studies examining body composition and metabolic profiles following injury include only men.[9–12] To the authors' knowledge, only two studies have examined the influence of sex on body composition in individuals with SCI. One study evaluated complete and incomplete SCI and utilized waist circumference and a single abdominal slice from computed tomography to assess central obesity.[13] However, both methods have only been validated as reliable techniques in predicting central obesity in the AB population.[13–15] The second study used the gold standard magnetic resonance imaging (MRI) technique to quantify the differences in VAT and SAT between age, time since injury, level of injury matched men and women with SCI. The authors demonstrated that men with SCI have 1.8–2.6 times greater the amount of VAT compared to women with SCI.[16] Moreover, increase in VAT negatively impact lipid metabolism after SCI.[16] Despite the strong study design, a caveat of this study is the small sample size that is likely masked the sex effect on the cardiometabolic outcomes after SCI.

Truncal or central obesity, characterized by increasing waist circumference and VAT, is currently considered inflammatory in nature and marked by chronic, low-grade inflammation.[8] The accumulation VAT modifies the endocrine and metabolic functions of the tissue and is a major risk factor for cardiometabolic dysfunction.[6,10] Adipose tissues releases a number of signaling molecules, called proinflammatory adipokines, which are capable of activating intracellular stress signaling pathways that interfere with homeostatic mechanisms.[3,17] VAT is noted to directly release many proinflammatory adipokines, including tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), plasminogen activator inhibitor-1 (PAI-1), and thrombin activatable fibrinolysis inhibitor-1 (TAFI-1).[6,18,19] In the SCI and AB populations, many of these adipokines are elevated with central obesity and contribute to systemic and vascular inflammation.[6,20,21] In both obese SCI and AB participants, IL-6 was higher than a non-obese healthy control group, and in the participants with SCI, IL-6 significantly correlated with fasting plasma insulin.[17] Moreover, in chronic SCI, plasma levels of PAI-1 and markers of central obesity positively correlated, while abdominal sagittal diameter was positively related with high sensitivity c-reactive protein (hs-CRP),[22–25] a biomarker of systemic inflammation secreted mainly by the liver that is elevated in chronic SCI.[26] These proinflammatory adipokines are consequently thought to influence whole-body metabolism and to be the link in the pathogenesis of central obesity and cardiometabolic dysfunction.[3] Currently, the influence of sex on proinflammatory adipokines remains poorly understood in individuals with and without SCI. However, evidence has shown estrogen diminishes inflammatory signaling and improves insulin sensitivity, suggesting a relationship between sex and central obesity-induced inflammation.[4]

The purpose of the present study was to examine the influence of sex on the distribution of adipose tissue, especially VAT, and proinflammatory adipokine and cardiometabolic profiles in individuals with motor complete SCI. Moreover, we aimed to determine whether a sex-based dichotomy existed among the correlations between depot of adipose tissue and proinflammatory adipokines.

## METHODS

### *Participants*

Forty-seven participants with chronic, traumatic motor complete SCI were included in this cross-sectional

**Table 1 Participant demographics by sex.**

| | Male (n = 38) | Female (n = 9) | P - Value |
|---|---|---|---|
| Age (y) | 44.9 ± 10.9 | 42.0 ± 13.5 | P = 0.405 |
| Height (cm) | 176.6 ± 8.0* | 163.7 ± 6.2 | P < 0.001 |
| Weight (kg) | 84.9 ± 19.7 | 74.1 ± 17.6 | P = 0.075 |
| Body mass index (kg/m$^2$) | 27.2 ± 5.8 | 27.8 ± 6.6 | P = 0.755 |
| Time since injury (y) | 15.2 ± 11.0 | 10.9 ± 11.1 | P = 0.203 |
| Level of injury | C4 – L1 | C4 – T11 | NA |

study and classified according to their sex (male: n = 38, female: n = 9; Table 1). Demographic information can be found in Table 1. All participants completed informed consent that was approved by the Institutional Review Board at the host institution.

Inclusion criteria included: (1) men and women from 18 to 65 years old, with maximum age chosen to avoid any confounding influences of age on body composition; (2) C4-L2 motor complete individuals (American Spinal Injury A & B[27]); and (3) at least one year post-SCI, as by this time body composition changes will be stabilized. Complete SCI was only studied to ensure a homogenous study sample and limit the potential influence of incomplete versus complete SCI on body composition.[12,28] Exclusion criteria were as follows: (1) smokers or alcohol abusers, (2) those with any known orthopedic limitations and/or uncontrolled spasticity, (3) hypothyroidism, (4) preexisting renal or cardiometabolic disease, and/or infection/infectious disease; (5) deep vein thrombosis or uncontrolled autonomic dysreflexia within the past three months, (6) pressure injuries greater than grade II, and/or (7) individuals with incompatible material for MRI (i.e., stents, valves, rods, etc.) implanted for medical purposes.

### *Magnetic resonance imaging*

Non-contrast MRI was obtained of the abdominopelvic region with a 3-T magnet (Philips, Amsterdam, the Netherlands) whole-body scanner. T1-weighted imaging was completed using a fast spin-echo sequence with an axial in-phase/out-phase, a field of view of 30 × 40 cm, with a repetition time of 7.96 ms and an echo time of 2.38 ms, a 240 × 320 matrix size, flip angle of 10, and 1 excitations 1. Participants were assisted into the supine position on the MRI table and their distal limbs were strapped together to ensure a neutral position and prevent any spasticity that could lead to image artifact. Scans were performed with the participants' upper limbs above their head or across their chest if participants had a limited range of motion. Four mm thick transverse slices were acquired every four mm from the xiphoid process to the head of the femur. Using the umbilicus, the L4-L5 intervertebral disc was identified and all images were obtained in a series of two stacks superior and inferior to this intervertebral disc.[12,28] The first series of images extended superiorly from L4-L5 to the xiphoid process, while the second series of images extended inferiorly from L4-L5 to the femoral heads. During the scan, participants were asked to deeply inhale and hold their breath for 10 to 15 seconds to limit artifact caused by respiratory motion typically associated with abdominopelvic MRI acquisition. The use of two stacks of images reduced the breath holding time required for the study participants, especially those with higher SCI. Participants were instructed to remain motionless, were provided a blanket to help maintain normal body temperature and prevent spasticity, and were provided earplugs to reduce the noise from the MRI magnet.[10,29–31]

All MRI images were downloaded to a disk and analyzed using ImageJ (National Institutes of Health, Bethesda, Maryland, USA, https://imagej.nih.gov/ij). Cross-sectional area was automatically calculated via the imaging software by summing the pixels of the tissue and multiplying the pixel sum by the pixel surface area (field of view divided by matrix size squared). Volume was computed as the product of the tissue CSA and the image slice thickness and inter-slice space. Visual distinction was used to determine SAT and VAT based on their anatomical depots as previously described[10] and the volumes were summed together from consecutive slices for each depot. Total trunk adipose tissue (TTAT) was calculated by summing the consecutive volumes of the VAT and SAT slices of each participant. A ratio of VAT to SAT was calculated.[32] We chose to examine adipose tissue volume as it has been reported to accurately reflect intraabdominal adipose tissue compared to CSA.[12]

### *Inflammatory and cardiometabolic assessment*

Participants were admitted to the clinical research center at the host institution for a 12-hour fast that was followed by the collection of plasma proinflammatory adipokines and carbohydrate and lipid profiles. Ten ml of blood was collected for assessment of inflammatory biomarkers (TNF-α, IL-6, PAI-1, TAFI, and hs-CRP) and lipids. A standard intravenous glucose tolerance test (IVGTT) was performed to determine glucose effectiveness ($S_G$) and insulin sensitivity ($S_I$) according to previously published methods.[33] Briefly, an indwelling catheter with an intravenous saline drip (0.9% NaCl) was placed in an antecubital vein while another intravenous line was placed on a contralateral hand vein. These lines were used to assist with the infusion of glucose and blood sampling throughout the IVGTT. Glucose samples were obtained at –6, –4, –2, 0, 2, 3, 4, 5, 6, 8, 10, 12, 14, 16, 19, 22, 23, 24, 25, 27, 30, 35, 40, 50, 60, 70, 80, 90, 100, 120, 140, 160, and 180 minutes after the rapid injection of glucose (0.3 g/kg over 30 seconds at time zero). Twenty minutes following the glucose injection, an insulin bolus (0.02 U/kg) was injected to determine $S_I$. Heart rate and blood pressure were evaluated at 22, 23, and 24 minutes of the IVGTT. Fasting plasma glucose was calculated as the average of –6, –4, –2, and 0

minutes before the administration of the bolus of glucose. $S_I$ and $S_G$ are computed from a least squares fitting of the temporal pattern of insulin and glucose during the IVGTT using the Minimal Model System (MinMod Inc., Pasadena, California, USA).

TNF-α, IL-6, PAI-1, (R&D Systems Inc., Minneapolis, Minnesota, USA) TAFI (Kamiya Biomedical Company, Seattle, Washington, USA), and hs-CRP (ALPCO, Salem, New Hampshire, USA) plasma concentrations were measured using a commercially available high-sensitivity enzyme-linked immunosorbent assay. Fasting blood glucose (Wako Chemical USA Inc., Richmond, Virginia, USA), triglycerides (TG; Sigma-Aldrich Co. LCC, St Louis, Missouri, USA), total cholesterol (TC), low-density lipoprotein-cholesterol (LDLC), and high-density lipoprotein-cholesterol (HDLC) (Thermo DMA, Austin, Texas, USA) were determined using commercially available colorimetric assays.

### *Statistical analysis*

All data were checked for normality with the Shapiro-Wilk test and box-plots. Values that did not meet parametric standards were log-transformed as this is frequently seen with plasma adipokines and metabolic parameters.[34] Differences between sexes were assessed with the Mann–Whitney independent U-test, while Spearman rho correlations were used to assess the relationships between adipose tissue depot and proinflammatory adipokines. Secondary analysis was performed using analysis of covariance (ANCOVA) to covary for the effect of height on VAT and SAT distributions between both sexes. All values are presented as means ± standard deviation and are untransformed. With a calculated effect size of $d = 1.38$ found for VAT, two-tailed $\alpha = 0.05$, and assuming 80% power, sample size for each test was calculated to be 10 per group. Currently, with our given sample size per group we have 83% power. All analyses were computed using SPSS 24.0 (IBM, Armonk, New York), while G*Power (Version 3.1.9.2; Franz, Universitat Kiel, Germany) was used to compute power.[35]

## RESULTS

Demographic characteristics did not differ between sexes except for height where male participants with SCI were about thirteen cm taller than female participants with SCI ($P < 0.001$; Table 1). However, height differences are not uncommon when evaluating sexes.[36] Male participants with SCI had a significantly greater volume of VAT and VAT:SAT ratio compared with females ($P \leq 0.002$), while female participants with SCI had a significantly greater volume of SAT compared to males ($P < 0.001$; Table 2). No difference was noted in TTAT between groups ($P = 0.341$). In the ANCOVA comparing VAT, SAT, and the VAT:SAT ratio between the male and female participants with SCI, there was a significant overall group effect (VAT: $F = 5.53$, degrees of freedom = 1.00, $P = 0.023$; SAT: $F = 12.66$, degrees of freedom = 1.00, $P = 0.001$; and VAT:SAT ratio: $F = 14.51$, degrees of freedom = 1.00, $P < 0.001$) after using height as a covariate.

**Table 2 Adipose tissue by sex.**

| | Male | Female | P - Value |
|---|---|---|---|
| SAT* volume (mL) | 3517.7 ± 1538.7 | 6064.5 ± 2800.0 | P = 0.001 |
| VAT† volume (mL) | 2541.4 ± 1323.2 | 1053.5 ± 762.4 | P = 0.002 |
| TTAT‡ volume (mL) | 6085.7 ± 2472.6 | 7060.2 ± 3170.7 | P = 0.341 |
| VAT:SAT ratio | 0.75 ± 3.2 | 0.17 ± 0.1 | P < 0.001 |

*SAT, subcutaneous adipose tissue.
†VAT, visceral adipose tissue.
‡TTAT, total trunk adipose tissue.

**Table 3 Inflammatory adipokine and cardiometabolic profiles by sex.**

| | Male | Female | P - Value |
|---|---|---|---|
| Tumor necrosis factor-α (pg/ml) | 17.8 ± 36.8 | 8.7 ± 0.9 | P = 0.400 |
| Interleukin-6 (pg/ml) | 7.8 ± 11.0 | 4.2 ± 3.2 | P = 0.277 |
| Plasminogen activatable inhibitor-1 (ng/ml) | 92.1 ± 66.9 | 62.8 ± 60.6 | P = 0.167 |
| Thrombin activatable fibrinolysis inhibitor-1 (ng/ml) | 10.14 ± 2.3 | 12.4 ± 10.2 | P = 0.131 |
| High-sensitivity c-reactive protein (mg/ml) | 8.7 ± 7.9 | 6.0 ± 4.7 | P = 0.268 |
| Systolic blood pressure (bmp) | 115.2 ± 14.1 | 109.8 ± 14.2 | P = 0.220 |
| Diastolic blood pressure (bmp) | 70.1 ± 10.3 | 67.5 ± 12.3 | P = 0.235 |
| Fasting glucose (mg/dL) | 99.2 ± 28.1 | 93.7 ± 12.1 | P = 0.495 |
| Glucose effectiveness | 0.02 ± 0.01 | 0.02 ± 0.01 | P = 0.569 |
| Insulin sensitivity | 7.8 ± 23.1 | 3.9 ± 3.4 | P = 0.573 |
| Triglycerides (mg/dL) | 120.9 ± 49.5 | 97.8 ± 65.5 | P = 0.236 |
| Total cholesterol (mg/dL) | 155.9 ± 32.3 | 153.8 ± 19.8 | P = 0.882 |
| Low density lipoprotein-cholesterol (mg/dL) | 95.2 ± 30.0 | 89.2 ± 14.0 | P = 0.484 |
| High density lipoprotein-cholesterol (mg/dL) | 34.3 ± 8.0 | 43.2 ± 7.6 | P < 0.001 |
| Total cholesterol/HDLC ratio | 4.7 ± 1.3 | 3.6 ± 0.4 | P = 0.003 |

**Table 4 Spearman rho correlations between adipose tissue and proinflammatory adipokines by sex.**

| Male | TNF-α | IL-6 | PAI-1 | TAFI-1 | hs-CRP |
|---|---|---|---|---|---|
| SAT volume | 0.311 | 0.017 | 0.296 | -0.014 | 0.292 |
| VAT volume | 0.347* | 0.168 | 0.278 | -0.121 | 0.229 |
| VAT/SAT ratio | 0.146 | 0.093 | 0.168 | -0.112 | -0.031 |
| Female | | | | | |
| SAT volume | 0.168 | -0.095 | 0.738* | -0.476 | 0.238 |
| VAT volume | 0.577 | -0.100 | 0.600 | 0.200 | 0.683* |
| VAT/SAT ratio | 0.647 | -0.238 | 0.310 | 0.405 | 0.762* |

*$P < 0.05$.
hs-CRP, High-sensitivity c-reactive protein; IL-6, interleukin-6; PAI-1, plasminogen activatable inhibitor-1; SAT, subcutaneous adipose tissue; TAFI-1, thrombin activatable fibrinolysis inhibitor-1; TNF- α, tumor necrosis factor-α; VAT, visceral adipose tissue.

A comparison between proinflammatory adipokines and cardiometabolic profiles between the sexes can be found in Table 3. Proinflammatory adipokines did not differ between the groups ($P > 0.05$); however, males generally showed unfavorable profiles compared to female participants with SCI. HDLC and the TC:HDLC ratio were significantly greater in male participants with SCI compared with female participants with SCI ($P < 0.05$). All other cardiometabolic profiles were not significantly different between sexes ($P > 0.05$; Table 3).

Correlations between adipose tissue depots and proinflammatory adipokines by sex are presented in Table 4. Among male participants with SCI, VAT volume significantly correlated with TNF-α ($\rho = 0.347$, $P < 0.05$). In female participants with SCI, SAT volume correlated with PAI-1 ($\rho = 0.738$, $P < 0.05$) and both VAT volume and the VAT:SAT ratio correlated with hs-CRP ($\rho = 0.683$ and $\rho = 0.762$, $P < 0.05$, respectively). All other correlations were not significant (Table 4).

## DISCUSSION

Deterioration in body composition and its association with negative cardiometabolic profiles are well documented following SCI.[1,9,12,37,38] However, much of the literature examining the influence of SCI on body composition and cardiometabolic profiles fails to consider the influences of sex and adipose tissue-derived inflammatory adipokines. This is despite emerging research in the AB population beginning to demonstrate the role of sex in body composition and cardiometabolic health.[3,4] Therefore, the aim of this study was to evaluate the influence of sex on adipose tissue and its role in inflammatory adipokines and cardiometabolic profiles following SCI. The main findings from the present study demonstrate a dichotomy in central adiposity and proinflammatory adipokines in men and women with SCI. Specifically, male participants with SCI demonstrated a significantly greater VAT volume and VAT:SAT ratio, while female participants had a significantly greater volume of SAT and similar TTAT to male participants with SCI. Moreover, unique sex-based correlations between adipose tissue and proinflammatory adipokines were present among our participants, suggesting sex-specific characteristics of central adiposity may promote unique inflammatory profiles.

In the present study, we have demonstrated significantly greater VAT volume in men than women and greater SAT volume in women than men with SCI. In addition, similar TTAT was present between both sexes. In a recent study in motor complete SCI, the authors demonstrated similar results using MRI CSA in men and women with SCI.[16] In a heterogeneous sample of complete and incomplete SCI, researchers demonstrated that women with SCI have greater total central adiposity compared to men.[13,39] In AB literature, sex dimorphism in adipose tissue distribution is documented[3,4] and is associated with whole-body metabolic health. In general, women typically have greater adiposity than men throughout their lifetimes; however, men have greater visceral adiposity, which is routinely documented to carry greater cardiometabolic risk.[3,4] In contrast, women are characterized by less VAT and higher volumes of SAT. Some evidence suggests that the distribution of adipose tissue is dependent on sex hormones.[3,4,16] In AB menopausal and postmenopausal women, who have lower circulating estrogen levels, visceral adiposity increases.[3,40,41] When these women are placed on hormone replacement therapy, waist circumference, a marker of central adiposity in the AB population, decreases.[42,43] Estrogen replacement has also been shown to improve lipid profiles by lowering LDLC and raising HDLC profiles, as well as preventing osteoporosis.[44] Moreover, when aging AB men were placed on testosterone therapy, researchers noted decreases in VAT and increases in muscle mass.[45] Thus, this may indicate a role for estrogen and testosterone in the storage and distribution of adipose tissue and highlights the potential role of sex hormones in the management of central obesity and obesity-related complications following SCI.

The significant correlation between VAT and TNF-α suggests that with increasing visceral adiposity men with SCI experience a greater amount of systemic inflammation. This may potentially lead to a greater amount of lipid dysfunction as we observed in the present study. TNF-α has been documented to alter lipid and carbohydrate homeostasis, as previously demonstrated in the AB literature.[46] We demonstrated a significantly elevated TC:HDLC ratio in male participates with SCI, as well as a significantly higher HDLC

in female participants. These results mirror previous studies by Schmid *et al.*[47] and Edwards *et al.*[48] showing men with SCI had elevated LDLC and TG, as well as lower HDLC compared to female participants with SCI. This may be a result of greater volume of VAT in males leading to an over expression of proinflammatory adipokines and subsequently greater endothelial lipase production, which is considered important for HDLC clearance from the vascular tree.[49] Bauman *et al.*[38] similarly found no difference in plasma glucose between men and women with SCI; however, the authors showed plasma insulin in men with SCI was significantly elevated at 30, 60, and 90 minutes during an oral glucose tolerance test (OGTT), suggesting a relative state of insulin resistance in men with SCI. In the present study, we did not find any significant differences in glucose effectiveness or insulin sensitivity between men and women with SCI. This difference in results between our study and Bauman *et al.*,[38] may be twofold: first, OGTT is less accurate than IVGTT and may have led to a false positive finding;[50] and second, female participants with SCI demonstrated a greater SAT volume, which has been reported to possess greater carbohydrate and lipid storage capabilities in the AB population.[3] In the study by Bauman *et al.*,[38] the authors did not differentiate adipose tissue by depot.

This study is not without limitations. First, the sample size of female participants was relatively small compared to the group of males with SCI. This may have resulted in a type-two error and could explain the failure to reach statistical significance in specific analyses between groups. However, such small female sample sizes are not uncommon in SCI research.[51,52] Second, we did not assess physical activity level or estrogen and testosterone levels which are thought to influence adipose tissue depots and lipid storage.[3] Third, in our study, we assessed circulating levels of proinflammatory adipokines and can therefore not accurately account for other sources of release. However, biopsies of adipose tissue, especially from visceral depots, were not practical for our study and proinflammatory adipokines are not primarily released from SAT.[32,53] Previous literature has also shown that methods used to process adipose tissue biopsies can result in variable concentrations of proinflammatory profiles, making reproducibility and comparisons to existing SCI and AB clinical literature difficult.[54] Lastly, the lack of a control group and sex- and aged matched participants, as well as the cross-sectional study design, makes predictions as to the prognostic and diagnostic value of the evaluated markers and long-term implications difficult. Therefore, prospective studies assessing the use of dietary and exercise intervention are required.

## CONCLUSION

In summary, this study suggests distinctive patterns of central adiposity in men and women with SCI given the relatively distinctive storage locations of adipose tissue and their effect on inflammatory and cardiometabolic profiles. Additionally, this study highlights the importance of assessing adipose tissue by depot in future studies as the TTAT between male and females with SCI was similar while VAT and SAT volumes were different between groups. Greater VAT in males with SCI may lead to generally greater amounts of cardiometabolic dysfunction via the elevation of proinflammatory adipokines. Future research with a larger sample size needs to evaluate the influence of dietary restriction and exercise on sex-based adiposity, as well as inflammatory and cardiometabolic profiles in chronic motor complete SCI.

## Disclaimer statements

**Contributors** GJF devised the project framework, the conceptual ideas, conducted the appropriate analyses, and wrote the initial manuscript draft. ASG, DRD, and DRG collected the date. ASG and ASB contributed to the statistical analyses. All authors contributed to and reviewed the final version of the manuscript.

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**Ethics approval** None.

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## References

1 Gorgey AS, Dolbow DR, Dolbow JD, Khalil RK, Castillo C, Gater DR. Effects of spinal cord injury on body composition and metabolic profile - part I. J Spinal Cord Med 2014;37:693–702.
2 Farkas GJ, Gater DR. Neurogenic obesity and systemic inflammation following spinal cord injury: a review. J Spinal Cord Med 2017:1–10.
3 White UA, Tchoukalova YD. Sex dimorphism and depot differences in adipose tissue function. Biochim Biophys Acta 2013;1842(3):377–92.
4 Fuente-Martín E, Argente-Arizón P, Ros P, Argente J, Chowen JA. Sex differences in adipose tissue: It is not only a question of quantity and distribution. Adipocyte 2013;2(3):128–34.
5 Mauvais-Jarvis F. Sex differences in metabolic homeostasis, diabetes, and obesity. Biol Sex Differ. 62015.
6 Jung UJ, Choi M-S. Obesity and its Metabolic Complications: The Role of Adipokines and the Relationship between Obesity, Inflammation, Insulin Resistance, Dyslipidemia and Nonalcoholic Fatty Liver Disease. Int J Mol Sci 2014;15:6184–223.
7 Spinal Cord Injury (SCI) 2016 Facts and Figures at a Glance. J Spinal Cord Med 2016;39(4):493–4.

8 Curtin CM, Suarez PA, Di Ponio LA, Frayne SM. Who are the women and men in Veterans Health Administration's current spinal cord injury population? J Rehabil Res Dev 2012;49(3):351–60.
9 Gorgey AS, Mather KJ, Poarch HJ, Gater DR. Influence of motor complete spinal cord injury on visceral and subcutaneous adipose tissue measured by multi-axial magnetic resonance imaging. J Spinal Cord Med 2011;34:99–109.
10 Gorgey AS, Gater DR. Regional and relative adiposity patterns in relation to carbohydrate and lipid metabolism in men with spinal cord injury. Appl Physiol Nutr Metab 2011;36:107–14.
11 Neto FR, Lopes GH. Body composition modifications in people with chronic spinal cord injury after supervised physical activity. J Spinal Cord Med 2011;34(6):586–93.
12 Gorgey AS, Mather KJ, Gater DR. Central adiposity associations to carbohydrate and lipid metabolism in individuals with complete motor spinal cord injury. Metab Clin Exp 2011;60:843–51.
13 Edwards LA, Bugaresti JM, Buchholz AC. Visceral adipose tissue and the ratio of visceral to subcutaneous adipose tissue are greater in adults with than in those without spinal cord injury, despite matching waist circumferences. Am J Clin Nutr 2008;87:600–7.
14 Kullberg J, Brandberg J, Angelhed JE, Frimmel H, Bergelin E, Strid L, *et al*. Whole-body adipose tissue analysis: comparison of MRI, CT and dual energy X-ray absorptiometry. Br J Radiol 2009;82(974):123–30.
15 Clasey J, Gater D. Body Composition Assessment in Adults with Spinal Cord Injury. Top Spinal Cord Inj Rehabil 2007;12:8–19.
16 Gorgey AS, Farkas GJ, Dolbow DR, Khalil RE, Gater DR. Gender Dimorphism in Central Adiposity May Explain Metabolic Dysfunction After Spinal Cord Injury. Pm r 2017.
17 Gater DR. Obesity after spinal cord injury. Phys Med Rehabil Clin N Am 2007;18:333–51.
18 Katsareli EA, Dedoussis GV. Biomarkers in the field of obesity and its related comorbidities. Expert Opin Ther Targets 2014;18:385–401.
19 You T, Arsenis NC, Disanzo BL, Lamonte MJ. Effects of exercise training on chronic inflammation in obesity : current evidence and potential mechanisms. Sports Med 2013;43(4):243–56.
20 Makki K, Froguel P, Wolowczuk I. Adipose Tissue in Obesity-Related Inflammation and Insulin Resistance: Cells, Cytokines, and Chemokines. Int Sch Res Notices 2013;2013:e139239.
21 Bajzar L. Thrombin activatable fibrinolysis inhibitor and an antifibrinolytic pathway. Arterioscler Thromb Vasc Biol 2000;20(12):2511–8.
22 Manns PJ, McCubbin JA, Williams DP. Fitness, inflammation, and the metabolic syndrome in men with paraplegia. Arch Phys Med Rehabil 2005;86:1176–81.
23 Krause JS, DiPiro ND, Saunders LL, Newman SD, Banik NL, Park S. Allostatic Load and Spinal Cord Injury: Review of Existing Research and Preliminary Data. Top Spinal Cord Inj Rehabil 2014;20:137–46.
24 Hansen D, Dendale P, Beelen M, Jonkers RAM, Mullens A, Corluy L, *et al*. Plasma adipokine and inflammatory marker concentrations are altered in obese, as opposed to non-obese, type 2 diabetes patients. Eur J Appl Physiol 2010;109:397–404.
25 Roytblat L, Rachinsky M, Fisher A, Greemberg L, Shapira Y, Douvdevani A, *et al*. Raised Interleukin-6 Levels in Obese Patients. Obes Res 2000;8:673–5.
26 Maruyama Y, Mizuguchi M, Yaginuma T, Kusaka M, Yoshida H, Yokoyama K, *et al*. Serum leptin, abdominal obesity and the metabolic syndrome in individuals with chronic spinal cord injury. Spinal Cord 2008;46:494–9.
27 Kirshblum SC, Burns SP, Biering-Sorensen F, Donovan W, Graves DE, Jha A, *et al*. International standards for neurological classification of spinal cord injury (Revised 2011). J Spinal Cord Med 2011;34:535–46.
28 Doherty JG, Burns AS, O'Ferrall DM, Ditunno JF, Jr. Prevalence of upper motor neuron vs lower motor neuron lesions in complete lower thoracic and lumbar spinal cord injuries. J Spinal Cord Med 2002;25(4):289–92.
29 Ross R, Rissanen J. Mobilization of visceral and subcutaneous adipose tissue in response to energy restriction and exercise. Am J Clin Nutr 1994;60(5):695–703.
30 Ross R, Rissanen J, Hudson R. Sensitivity associated with the identification of visceral adipose tissue levels using waist circumference in men and women: effects of weight loss. Int J Obes Relat Metab Disord 1996;20(6):533–8.
31 Ross R, Rissanen J, Pedwell H, Clifford J, Shragge P. Influence of diet and exercise on skeletal muscle and visceral adipose tissue in men. J Appl Physiol (1985) 1996;81(6):2445–55.
32 Gorgey AS, Wells KM, Austin TL. Adiposity and spinal cord injury. World J Orthop 2015;6:567–76.
33 Shuster A, Patlas M, Pinthus JH, Mourtzakis M. The clinical importance of visceral adiposity: a critical review of methods for visceral adipose tissue analysis. Br J Radiol. 85 2012. p. 1–10.
34 Gorgey AS, Harnish CR, Daniels JA, Dolbow DR, Keeley A, Moore J, *et al*. A report of anticipated benefits of functional electrical stimulation after spinal cord injury. J Spinal Cord Med 2012;35:107–12.
35 Faul F, Erdfelder E, Buchner A, Lang AG. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. Behav Res Methods 2009;41(4):1149–60.
36 Tuck MK, Chan DW, Chia D, Godwin AK, Grizzle WE, Krueger KE, *et al*. Standard operating procedures for serum and plasma collection: early detection research network consensus statement standard operating procedure integration working group. J Proteome Res 2008;8(1):113–7.
37 Spungen AM, Adkins RH, Stewart CA, Wang J, Pierson RN, Waters RL, *et al*. Factors influencing body composition in persons with spinal cord injury: a cross-sectional study. J Appl Physiol (1985) 2003;95:2398–407.
38 Bauman WA, Adkins RH, Spungen AM, Waters RL. The effect of residual neurological deficit on oral glucose tolerance in persons with chronic spinal cord injury. Spinal Cord 1999;37(11):765–71.
39 Fryar CD, Gu Q, Ogden CL. Anthropometric reference data for children and adults: United States, 2007–2010. Vital Health Stat 2012(252):1–48.
40 Piche ME, Lapointe A, Weisnagel SJ, Corneau L, Nadeau A, Bergeron J, *et al*. Regional body fat distribution and metabolic profile in postmenopausal women. Metabolism 2008;57(8):1101–7.
41 Lizcano F, Guzmán G. Estrogen Deficiency and the Origin of Obesity during Menopause. Biomed Res Int 2014;2014.
42 Munoz J, Derstine A, Gower BA. Fat distribution and insulin sensitivity in postmenopausal women: influence of hormone replacement. Obes Res 2002;10(6):424–31.
43 Yuksel H, Odabasi AR, Demircan S, Koseoglu K, Kizilkaya K, Onur E. Effects of postmenopausal hormone replacement therapy on body fat composition. Gynecol Endocrinol 2007;23(2):99–104.
44 Lombardi G, Mondaini N, Macchiarella A, Del Popolo G. Female sexual dysfunction and hormonal status in spinal cord injured (SCI) patients. J Androl 2007;28(5):722–6.
45 Allan CA, Strauss BJ, Burger HG, Forbes EA, McLachlan RI. Testosterone therapy prevents gain in visceral adipose tissue and loss of skeletal muscle in nonobese aging men. J Clin Endocrinol Metab 2007;93(1):139–46.
46 Ouchi N, Parker JL, Lugus JJ, Walsh K. Adipokines in inflammation and metabolic disease. Nat Rev Immunol 2011;11(2):85–97.
47 Schmid A, Knöebber J, Vogt S, König D, Deibert P, Bültermann D, *et al*. Lipid Profiles of Persons With Paraplegia and Tetraplegia: Sex Differences. J Spinal Cord Med 2008;31(3):285–9.
48 Yarar-Fisher C, Chen Y, Jackson AB, Hunter GR. Body mass index underestimates adiposity in women with spinal cord injury. Obesity (Silver Spring, Md) 2013;21:1223–5.
49 Paradis ME, Badellino KO, Rader DJ, Deshaies Y, Couture P, Archer WR, *et al*. Endothelial lipase is associated with inflammation in humans. J Lipid Res 2006;47(12):2808–13.
50 Nadon GW, Little JA, Hall WE, O'Sullivan MO. A Comparison of the Oral and Intravenous Glucose Tolerance Tests in Non-Diabetic, Possible Diabetic and Diabetic Subjects. Can Med Assoc J 1964;91(26):1350–3.
51 Yarar-Fisher C, Chen YY, Jackson AB, Hunter GR. Body Mass Index Underestimates Adiposity in Women with Spinal Cord Injury. Obesity 2013;21(6):1223–5.
52 Beck LA, Lamb JL, Atkinson EJ, Wuermser L-A, Amin S. Body composition of women and men with complete motor paraplegia. J Spinal Cord Med 2014;37:359–65.
53 Mammi C, Calanchini M, Antelmi A, Cinti F, Rosano GM, Lenzi A, *et al*. Androgens and adipose tissue in males: a complex and reciprocal interplay. Int J Endocrinol 2012;2012.
54 Keustermans GC, Hoeks SB, Meerding JM, Prakken BJ, de Jager W. Cytokine assays: an assessment of the preparation and treatment of blood and tissue samples. Methods 2013;61(1):10–7.